In the United States Court of Federal Claims

STEPHANE AND ANTHONY FIORELLO, on behalf of their minor child, R.F., Petitioners, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	No. 17-1869V (Filed Under Seal: February 20, 2025. Reissued for Publication 3/10/2025)*

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Ryan Pohlman Miller, Trial Attorney, Torts Branch, Civil Division, U.S. Department of Justice, Washington, DC, with whom were Julia C. Collison, Assistant Director, Heather L. Pearlman, Deputy Director, C. Salvatore D'Alessio, Director, for Respondent.

OPINION AND ORDER

This case arises under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 ("Vaccine Act" or "the Act"). It is currently before the Court on the Petitioners' motion for review. Pet'rs' Mot. for Rev., ECF No. 85. Petitioners challenge Special Master Daniel T. Horner's decision that they failed to prove that the hepatitis B vaccine caused their son R.F. to experience chronic dysregulation of his immune system characterized by recurrent hypersensitive reactions to viral infections. See Decision of Spec. Mstr., ECF No. 83 [hereinafter "Dec."]; see also Fiorello v. Sec'y of Health & Hum. Servs., 2024 U.S. Claims LEXIS 2330, 2024 WL 4133302 (Fed. Cl. Spec. Mstr. Aug. 12, 2024).

For the reasons set forth below, the Court finds that the special master's decision was neither arbitrary and capricious, nor contrary to law. Petitioners' motion for review is therefore **DENIED**.

* Pursuant to Vaccine Rule 18(b), this opinion was initially filed on February 20, 2025, and the parties were afforded fourteen days to propose redactions. The parties did not propose any redactions and, accordingly, this Opinion is reissued in its original form for publication.

BACKGROUND

I. Medical History

On December 8, 2008, R.F., the third of a set of triplets, was born by cesarean section at 29 weeks. Pet'rs' Ex. 14, at 13, ECF No. 16-1. After his birth, R.F. was put in the NICU, where he was treated for respiratory distress syndrome, hyperbilirubinemia, choroid plexus cyst, retinopathy of prematurity, apnea, tachycardia, and feeding difficulties—all of which are common in premature births. Id. R.F. responded well to treatment and was discharged on January 20, 2009. Id. at 12. He experienced developmental delays common in premature births and by his five-year well visit had been diagnosed with fine and gross motor delays, a sensory processing disorder, attention deficit hyperactivity disorder, and mild anxiety. Pet'rs' Ex. 17, at 52–57, ECF No. 18-1.

On December 4, 2014, R.F. received his second dose of the hepatitis B vaccine. Pet'rs' Ex. 5, at 14, ECF No. 9-1.[1] About 23 hours later, on December 5, 2014, Pet'rs' Ex. 11, at 11, ECF No. 13-1, R.F. was taken to urgent care where he presented with "[a]ltered mental status with episodes of pallor," Pet'rs' Ex. 3, at 2, ECF No. 8-3. R.F. was described as "oriented to time, place and person" but it was noted that he "[i]ntermittently" became less responsive. Id. A full blood culture was not obtained "because infectious etiology was lower on the differential initially," but a complete blood count and a comprehensive metabolic panel were obtained. See id. at 2–3. The tests revealed an abnormally high white blood cell count which, according to the pediatrician who examined R.F., might "point towards infectious etiology or [might] represent stress response." Id. at 2. Otherwise, the results of R.F.'s exams, including a nonfocal exam and an electrocardiogram, were normal. Id.

After the urgent care examination, R.F. was transferred to a hospital emergency room. See id. at 4. The ambulance team described his "accident or illness" as "syncope and collapse," but noted that R.F.'s condition was improved and that he was alert when examined. Pet'rs' Ex. 11, at 1–2. R.F. was described as "warm, dry, pale in color" and "acting normal according to his mother." Id. at 4. At the hospital, at around 6:30 PM, he was described as "awake[,] alert[,] and oriented." Id. at 8. Blood tests revealed that his white blood cell count was continually improving. Id. at 12. The results of other examinations were normal. See id. at 8–15.

The hospital records also note that R.F. had been experiencing a cough with no associated fever since the second week in September. Id. at 13. Though no official diagnosis was provided, the attending doctor stated that "differential diagnosis includes syncope, seizure, or intercurrent illness not evident on . . . evaluation" and R.F. was discharged the same day around 10:30 PM with orders for a sleep-deprived electroencephalogram ("EEG") and a follow-up with his pediatrician. Id. at 12, 15, 22.

Several months later, on March 6, 2015, R.F. had a check-up with his pediatrician during which he presented with symptoms of an upper respiratory infection. See Pet'rs' Ex. 5, at 17–19.

[1] R.F. received his first dose of the hepatitis B vaccine on August 28, 2014. Pet'rs' Ex. 5, at 11; see also Pet'rs' Ex. 1, at 2–3, ECF No. 8-1.

R.F.'s mother reported to the pediatrician that he had experienced another incident on December 5, during which he was pale, cold, hypotonic, and less responsive than usual. Id. R.F. again recovered completely from the episode after a few hours. Id.; see also Pet'rs' Ex. 1., at 5.

The pediatrician diagnosed R.F. with an unspecified upper respiratory infection and a "hypotonic/hyporesponsive episode," and recommended ruling out a seizure disorder or other neurological problems. Pet'rs' Ex. 5, at 18. R.F.'s physical exam was otherwise normal. Id. at 17–19. Subsequently, on March 27, 2015, R.F. underwent an EEG. Pet'rs' Ex. 9, at 95–96, ECF No. 11-3. The EEG report noted R.F. had a history of migraine headaches but identified no other neurological issues. Id.

On April 2, 2015, R.F. consulted with Dr. John Oppenheimer, an allergy and immunology specialist. The purpose of the consultation was to provide Petitioners with direction regarding R.F.'s future vaccinations. Pet'rs' Ex. 2, at 2, ECF No. 8-2. Dr. Oppenheimer diagnosed R.F. with severe seasonal allergic rhinoconjunctivitis but did not formally diagnose R.F. with any condition related to his hypotonic/hyporesponsive episodes. Id. In his assessment, Dr. Oppenheimer wrote:

> Status post episode of hypotonia with systemic complaints following vaccination to hepatitis B. Certainly, it is easy to blame the hepatitis vaccine for this; however, mechanistically, this is by no means an allergic response. Thus, skin testing will not aid. This certainly appears to be potentially an immune response and may speak to why three months later he had another episode when questionably it was a viral related illness. I am [aware] that neurology is following and I wholeheartedly encourage continued follow up as obviously the differential is protean. Presently, they are looking for potential seizures or migraines as etiology; however, it would be nice to know what potential triggers may bring this about for future observation.

Id.

On May 18, 2015, R.F. was admitted to the Overlook Medical Center, with an admitting diagnosis of "other convulsions." Pet'rs' Ex. 9, at 7. He was assessed for "episodes concerning for seizures [with] pallor [and] limpness." Id. at 15. His recorded history described the two episodes discussed above as well as unrelated eye issues. Id. at 12. Upon the recommendation of a physician at the facility, R.F. was hospitalized for a 48-hour video EEG, which observed him both awake and asleep from May 18 to May 20, 2015. See id. at 31–32. The pediatric neurologist who conducted the exam noted R.F.'s eye issues during the exam, but the video EEG displayed normal, non-epileptic events. Id. at 16, 19, 31–32.

On May 25, 2017, R.F. paid a visit to Dr. Mercy Chong, complaining of a cough and fever. Pet'rs' Ex. 28, at 28–31, ECF No. 60-1. Dr. Chong reported that R.F. "goes into shock with every new virus," and noted that there had been an episode the preceding Saturday. Id. at 28. The doctor described these as "immune episodes," and noted that they "[s]eem to have started after starting Hep B Series" but that "[t]here is some disagreement between the specialists." Id. at 29–30. R.F. was assessed as having experienced "hypotensive episode[s]" with "unclear etiology." Id. at 31. The attending physician also noted that there were "no labs, results, notes to go on." Id.

Approximately two months later, on July 19, 2017, R.F. had a well-child visit with Dr. Jeffrey Siegel at North Scottsdale Pediatrics. See Pet'rs' Ex. 6, at 30–32, ECF No. 10-1. Petitioners reported that R.F. could not undergo anesthesia, have vaccinations, or take new medications. Id. They also informed the doctor that an "immunology specialist" who had evaluated R.F. thought that he had a hyperimmune reaction, which they believed was caused by the hepatitis B vaccine. Id.

In his assessment, Dr. Siegel opined that R.F. experienced an "immune hypersensitivity reaction by mechanism," and observed that the "very rare immune reaction seems to have been triggered by Hep B vaccine." Id. at 32. Dr. Siegel also noted that R.F.'s episodes "always self resolve[]," and that getting a genetics opinion had been discussed. Id. He referred R.F. to Dr. S. Reed Shimamoto, an allergist at San Tan Allergy & Asthma. Id.

On August 17, 2017, Petitioners consulted with Dr. Shimamoto for evaluation of an immune deficiency. Pet'rs' Ex. 4, at 4–9, ECF No. 8-4. Dr. Shimamoto noted "there has been concern about possible relationship [between] vaccinations and these episodes but they persist despite no recent vaccines." Id. at 6.

Dr. Shimamoto noted that the immunologist in New Jersey (presumably Dr. Oppenheimer) had used the term "[h]yper-immune response" and not "allergic reaction." Id. He observed that "no diagnosis has been made" but questioned how a vaccine could "break [R.F.'s] entire immune system." Id. He added that "[a]t this point, everyone is just kind of stuck and no real answer as to why, why did it start at age 5–6 and not a congenital type of problem." Id. at 6.

Dr. Shimamoto also provided comments on Dr. Oppenheimer's evaluation. He observed that Dr. Oppenheimer had conducted no tests. He further observed that Dr. Oppenheimer had deemed R.F. "hyper-immune," but that he (Dr. Shimamoto) was "not sure exactly what th[at] refers to." Id. at 5–6. Dr. Shimamoto recommended an immune screen as well as the record of vaccine responses from his infant series to check for a pattern of specific immune-related disease. Id. at 6.

On October 6, 2017, Petitioners took R.F. to Dr. Siegel, complaining of extreme pain in his left arm. Pet'rs' Ex. 6, at 28. X-rays were taken and revealed that R.F. had a fractured distal radius and ulna. See Pet'rs' Ex. 6, at 28–30, 40.[2]

A few days later, on October 10, 2017, R.F. was evaluated at Phoenix Children's sports medicine practice. The orthopedist noted that R.F.'s x-rays were concerning for osteopenia. Id. at 17–18. He referred R.F. to an endocrinologist, Dr. Madhia Shahid, who saw R.F. on November 9, 2017. Pet'rs' Ex. 7, at 25, ECF No. 11-1. Dr. Shahid noted that the "'shock' like episodes which [R.F.] gets 7-8 x year could be due to hypoglycemia," but his concern about chronic hypoglycemia was "very low." Id. at 25–26. Dr. Shahid also diagnosed R.F. with osteopenia. Id. at 25.

[2] R.F. had previously broken his arm on November 19, 2014, Pet'rs' Ex. 10, at 5, ECF No. 11-4, but reportedly that injury healed normally, see Pet'rs' Ex. 1, at 7.

On April 27, 2018, R.F. was evaluated for "suspected vaccination reaction" by Dr. Michael Daines, and Dr. Pamela Tongchinsub, an allergy and immunology fellow. Pet'rs' Ex. 21, at 3, ECF No. 30-1. Dr. Tongchinsub concluded that "since episodes occur without inci[t]ing incident of vaccines each time, his symptom constellation is unlikely . . . immunodeficiency or vaccine reaction." Id. Instead, she listed R.F.'s differential diagnoses as postural orthostatic tachycardia syndrome ("POTS"), mast cell, congenital heart disease, and idiopathic anaphylaxis, though she also noted the "vagueness of symptoms." Id.

Three years later, in April of 2021, R.F. underwent genetic testing which returned normal results. Pet'rs' Ex. 32, at 35–67, ECF No. 79-1. The geneticist listed the differential diagnoses as familial dysautonomia, other hypersensitivity reactions, POTS, abdominal migraines, and mitochondrial disorders, "among others." Id. at 54. A cardiologist evaluated R.F. on April 21, 2021, and reported that she "cannot think of any clear unifying cardiac etiology that would explain his symptoms," and opined that no cardiology follow up was necessary. Id. at 22.

Dr. Siegel saw R.F. for a wellness check on August 18, 2021, and again assessed R.F. with "immune hypersensitivity reaction by mechanism," with diagnostic code "T78.40XD: Allergy, unspecified, subsequent encounter." Pet'rs' Ex. 28, at 13–14. Dr. Siegel again recommended following up with Dr. Shimamoto for advice on further vaccination, id., but no later records were cited by the parties or the Special Master.

II. Proceedings Before the Special Master

On December 4, 2017, Petitioners, on behalf of R.F., filed a petition for compensation under the National Childhood Vaccine Injury Act of 1986. 42 U.S.C. §§ 300aa-1 to -34. See Pet., ECF No. 1. Petitioners claimed that R.F. had suffered an injury caused by the hepatitis B vaccine he received on December 4, 2014. Pet'rs' Mot. for Rev., at 1–2.

Over the next six years, Petitioners filed additional medical records, see ECF Nos. 8–11, 13–14, 16, 18, 28, 30, 60, 75, 79, and medical literature, see ECF No. 45. They also filed three reports prepared by their expert, Dr. Ravi Durvasula. See ECF Nos. 41, 49, 67. The Secretary filed his report under Vaccine Rule 4(c), see Resp't's Rep., ECF No. 24; see also RCFC App. B, Vaccine Rule 4(c). The Secretary also submitted two reports prepared by the government's expert, Dr. Hayley Gans, see ECF Nos. 46, 71. Petitioners filed an amended petition on September 5, 2018. Am. Pet., ECF No. 29.

On August 29, 2019, this case was reassigned to Special Master Daniel Horner. ECF No. 43. The parties jointly requested to forgo an entitlement hearing in favor of a ruling on the record. See ECF No. 59; see also Pet'rs' Mem. Supp. Pet., ECF No. 76; Resp't's Resp. to Pet'rs' Mem. Supp. Pet., ECF No. 81; Pet'rs' Reply Mem. Supp. Pet., ECF No. 81.

III. Decision of the Special Master

On August 12, 2024, Special Master Horner ruled that Petitioners were not entitled to an award of compensation. Dec. at 1. He found that, even assuming R.F.'s first episode of altered mental status and pallor was caused by the second dose of the hepatitis B vaccine he received, that injury was not compensable as it did not persist for six months nor result in either death or

surgical intervention. Id. at 17 (citing 42 U.S.C. § 300aa-11(c)(1)(D)(i)). Therefore, the special master explained, Petitioners' entitlement to compensation was dependent upon whether they could prove that the initial hypersensitivity reaction allegedly caused by the vaccine in turn caused R.F. to develop chronic immune system dysregulation. Id.

In resolving that issue, the special master applied the three-prong test for establishing causation set forth by the court of appeals in Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274 (Fed. Cir. 2005). Under that test, to show causation a petitioner must provide: (1) "a medical theory causally connecting the vaccination and the injury;" (2) "a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" and (3) a showing of a "temporal relationship between vaccination and injury." 418 F.3d at 1278. The special master held that Petitioners failed to satisfy any of the three prongs, and so failed to make a prima facie case that the hepatitis B vaccine caused R.F.'s alleged injury. Dec. at 21, 27–28.

IV. Motion for Review

Petitioners filed their motion for review of the special master's decision and a supporting memorandum on September 11, 2024. See Pet'rs' Mot. for Rev., ECF No. 85; Pet'rs' Mem. Supp. Mot. for Rev., ECF No. 88 [hereinafter Pet'rs' Mem.]. They argue that the special master's findings on each of the three Althen prongs were not in accordance with law.

The Secretary filed a response on October 9, 2024. Resp't's Resp. to Pet'rs' Mot. for Rev., ECF No. 90. The Secretary contends that Petitioners have not identified any reversible errors, that Petitioners are asking this Court to improperly reweigh the evidence in the record, and that the special master's decision was neither arbitrary and capricious, nor contrary to law. Id.

With the Court's leave, see ECF No. 93, Petitioners filed a reply brief on October 16, 2024. Pet'rs' Reply Mem. Supp. Mot. for Rev., ECF No. 92. The Court has determined that oral argument is unnecessary and that the case is ripe for disposition.

DISCUSSION

I. Jurisdiction

Congress established the National Vaccine Injury Compensation Program in 1986 to provide a no-fault compensation system for vaccine-related injuries and deaths. Figueroa v. Sec'y of Health & Hum. Servs., 715 F.3d 1314, 1316–17 (Fed. Cir. 2013). The Vaccine Act is remedial legislation that "should be construed in a manner that effectuates its underlying spirit and purpose." Id. (quoting Cloer v. Sec'y of Health & Hum. Servs., 675 F.3d 1358, 1362 (Fed. Cir. 2012) (en banc)).

A petition seeking compensation under the Vaccine Act is filed in the Court of Federal Claims, after which the Clerk of the Court forwards it to the chief special master for assignment to a special master. 42 U.S.C. § 300aa-11(a)(1). The special master to whom the petition is assigned "issue[s] a decision on such petition with respect to whether compensation is to be provided under the [Vaccine Act] and the amount of such compensation." Id. § 300aa-12(d)(3)(A).

The Vaccine Act grants the Court of Federal Claims jurisdiction to review the decisions of special masters with authority to:

> (A) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision,
>
> (B) set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law, or
>
> (C) remand the petition to the special master for further action in accordance with the court's direction.

42 U.S.C. § 300aa-12(e)(2); see also Vaccine Rule 27.

II. Standard of Review

The Court reviews a special master's legal determinations de novo, applying the "not in accordance with law" standard. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1321 (Fed. Cir. 2010); Althen, 418 F.3d at 1278–79. Judicial review of a special master's factual determinations, on the other hand, is circumscribed and "uniquely deferential." Milik v. Sec'y of Health & Hum. Servs., 822 F.3d 1367, 1376 (Fed. Cir. 2016) (quoting Hodges v. Sec'y of Health & Hum. Servs., 9 F.3d 958, 961 (Fed. Cir. 1993)). The court may only set aside a special master's factual determinations where they are arbitrary, capricious, and/or reflect an abuse of discretion. Moberly, 592 F.3d at 1321.

In conducting judicial review, the court does not reweigh the evidence, examine its probative value, or judge the credibility of the witnesses, for those "are all matters within the purview of the fact finder." Porter v. Sec'y of Health & Hum. Servs., 663 F.3d 1242, 1254 (Fed. Cir. 2011) (citing Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1349 (Fed. Cir. 2010)). Thus, if a special master "'has considered the relevant evidence of record, drawn plausible inferences[,] and articulated a rational basis for the decision,' then reversible error is 'extremely difficult to demonstrate.'" Milik, 822 F.3d at 1376 (quoting Hines v. Sec'y of Health & Hum. Servs., 940 F.2d 1518, 1528 (Fed. Cir. 1991)).

III. The Special Master's Finding that Petitioners Failed to Satisfy Althen Prong One

To establish entitlement to compensation under the Vaccine Act, a petitioner must prove by a preponderance of the evidence that the "illness, disability, injury, or condition" at issue was caused—or significantly aggravated—by a vaccine. See 42 U.S.C. §§ 300aa-11(c)(1), -13(a)(1).

For an on-table claim, causation is presumed if the petitioner can show that (1) they received a vaccination listed in the Vaccine Injury Table, 42 U.S.C. § 300aa-14, as revised by 42 C.F.R. § 100.3(a); and (2) they suffered the injury associated with that vaccine in the Table within the period of time prescribed by the Table. See Andreu ex rel. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1374 (Fed Cir. 2009) (citing 42 U.S.C. § 300aa-11(c)(1)(C)(i)).

There is no presumption of causation, however, for off-table claims like the one at issue in this case. For those claims, a petitioner must establish causation in fact by proving by preponderant evidence "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)). If a petitioner makes that showing, then the burden shifts to the government to "show by a preponderance of the evidence that the injury [wa]s due to factors unrelated to the vaccine." Broekelschen, 618 F.3d at 1342 (citing Doe v. Sec'y of Health & Hum. Servs., 601 F.3d 1349, 1351 (Fed. Cir. 2010)); see also 42 U.S.C. § 300aa-13(a)(1)(B).

As discussed above, in Althen, the court of appeals established a three-prong test petitioners must satisfy to meet their burden of proving causation by preponderant evidence. For the reasons set forth below, the Court concludes that the special master's finding that Petitioners failed to provide a sound and reliable medical theory causally connecting R.F.'s vaccination with his injury, as required under Althen prong 1, was neither arbitrary and capricious nor contrary to law. And, because failure to satisfy any one of the Althen prongs is fatal to a petitioner's case, the court finds it unnecessary to address Petitioners' challenges to the special master's finding that they also failed to satisfy prongs two and three. See DePena v. Sec'y of Health & Hum. Servs., 133 Fed. Cl. 535, 549 (2017), aff'd, 730 F. App'x 938 (Fed. Cir. 2018).

A. Petitioners' Medical Theory

Althen prong one requires petitioners to supply "a medical theory causally connecting the vaccination and the injury." Althen, 418 F.3d at 1278. The theory need not be "medically or scientifically certain," but it must be "supported by sound and reliable medical or scientific explanation." Knudsen ex rel. Knudsen, 35 F.3d 543, 548–49 (Fed. Cir. 1994); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (stating under prong one "a petitioner must provide a reputable theory" that connects the vaccine to the injury).

Petitioners' expert, Dr. Ravi Durvasula, reviewed R.F.'s medical records as well as several published articles that he found pertinent, and articulated Petitioners' theory of medical causation. See Pet'rs' Ex. 22, ECF No. 41-1; Pet'rs' Ex. 30, ECF No. 67-1.[3] Dr. Durvasula opined that after R.F. received his second dose of the hepatitis B vaccine, he experienced a hypersensitivity reaction characterized by leukocytosis, hypothermia, and hypotonia. Pet'rs' Ex. 22, at 4. Dr. Durvasula described R.F.'s reaction as "closely resembl[ing] a picture of septic

[3] Dr. Durvasula is board certified in internal medicine and infectious diseases. Pet'rs' Ex. 23, at 30, ECF No. 41-2. He completed a bachelor's degree in biology and a medical degree from McGill University a residency in internal medicine at Baylor College of Medicine, and a fellowship at Yale University School of Medicine in infectious diseases. Id. at 1. Dr. Durvasula is currently the Chairman of the Department of Medicine and the John W. Clark Endowed Professor of Medicine in the Department of Public Health Sciences at Loyola University Stritch School of Medicine. Id. at 1. He has published 75 peer-reviewed manuscripts and book chapters, over 90 peer-reviewed abstracts and conference proceedings, and five books. Id. at 5–14.

shock," and "a clear systemic inflammatory response to vaccination." Id. He observed that "[e]tiologies such as bacterial sepsis, seizures, or cardiovascular disease were excluded." Id. Therefore, Dr. Durvasula found the "most likely cause" of R.F.'s symptoms was "an exaggerated immune response to the recombinant hepatitis B vaccine." Id.

Dr. Durvasula observed that after this initial reaction, which he attributed to the vaccine, R.F. continued to experience similar episodes several times per year. Id. These subsequent episodes, he theorized, were "all presumably triggered by viral illnesses." Id. Dr. Durvasula acknowledged that there was "no specific diagnostic test" that could prove an association between the vaccine, a hyperimmune reaction, and subsequent hyperimmune reactions to viral illnesses, and that R.F. was experiencing a complication that was "very rare." Id. Nonetheless, he opined, "the link between the vaccine, subsequent viral challenges and a severely exaggerated immune cascade resembling shock is plausible." Id.

Dr. Durvasula explained that "the activation of the immune system, the very basis for the use of vaccines, can become dysregulated." Id. He stated that "several triggers—medications, autoimmune signals and infectious pathogens—play etiologic roles." Id. According to Dr. Durvasula, "[c]ommon respiratory viruses that had little effect on [R.F.] prior to [his] hepatitis B vaccination became triggers following [his] exposure." Id. His "pattern of immune reactivity to viral infections," Dr. Durvasula further noted, was "predictable and consistent." Id.

Dr. Durvasula stated that "such highly exaggerated responses have been reported in the literature," and that "abnormal profiles of immunity, though rare, are [also] described" in the medical literature. Id. (citing L. Beretta et al., Churg-Strauss Vasculitis with Brain Involvement Following Hepatitis B Vaccination, 19 Clinical & Experimental Rheumatology 757 (2001) (Pet'rs' Ex. 25, ECF No. 45-2); Nancy Agmon-Levin et al., Vaccines and Autoimmunity, 5 Nature Revs. Rheumatology 648 (2009) (Pet'rs' Ex. 26, ECF No. 45-3)). He also took note of Dr. Shahid's October 2017 finding that R.F. had diffuse osteopenia. Id. at 5. According to Dr. Durvasula, this finding provided a further reason to suspect immune dysregulation given R.F.'s age and the association between chronic immunologic diseases and osteopenia, bone abnormalities, and risk of fracture. Id.

Dr. Durvasula cited Dr. Oppenheimer's report in support of his theory. Specifically, he noted, Dr. Oppenheimer referred to R.F.'s initial episode as a "hyper-immune reaction, triggered by the second dose of the hepatitis B vaccine." Id. at 4 (quoting Pet'rs' Ex. 2, at 2–3). Dr. Oppenheimer also opined that the immune reaction "may speak to why three months later he had another episode when questionably it was a viral related illness." Id. (quoting Pet'rs' Ex. 2, at 2–3).

Dr. Durvasula also cited the observations of Dr. Siegel, R.F.'s treating physician. Id. Dr. Siegel stated that R.F. had experienced an "immune hypersensitivity reaction by mechanism," and a "very rare immune reaction [that] seems to have been triggered by Hep B vaccine." Id. (quoting Pet'rs' Ex. 6, at 32).

Based on the foregoing, Dr. Durvasula concluded that "vaccination with recombinant antigens to confer immunity to hepatitis B is the likely cause of [R.F.'s] recurrent sepsis-like, inflammatory response to viral infections." Id. at 5. He characterized R.F.'s immune system as in

a state of "dysregulation." Id. And, he opined, although "diagnostic testing for such a response is not in the realm of standard clinical care," that fact "should not detract from the plausibility of this association." Id.

B. The Government's Response

Dr. Hayley Gans prepared an expert report for the government. Resp't's Ex. A, ECF No. 46-1.[4] She concluded that Dr. Durvasula's theory of causation lacked a reliable scientific basis.

Preliminarily, Dr. Gans observed that "no chronic conditions [have been] associated with [the] Hepatitis B vaccine." Id. at 5. She also noted that the evidence Dr. Durvasula cited to show a relationship between the hepatitis B vaccine and R.F.'s initial episode was temporal and not causal in nature. Id. Dr. Gans stated that the passage of time since the initial December 2014 episode made it less reasonable to assume that the vaccine caused the episode, because R.F. continued to experience similar episodes that were triggered by other "inciting events." Id. Dr. Gans stated that "what is clear is that over time, as RF has experienced more episodes and more evaluations have occurred, his treating physicians have begun to understand RF's chronic condition better." Resp't's Ex. C, at 1, ECF No. 71-1. "Over time," Dr. Gans observed, "the allergy/immunology physician, using all of the clinical and laboratory information, concluded that RF did not have anaphylaxis, [systemic inflammatory response syndrome ("SIRS")] and hyperimmune response;" "that the Hepatitis B vaccine that had initially been a consideration given the temporal relationship to the first episode was not the 'cause' of the recurrent episodes;" and "that these recurrent episodes would occur with many different triggers."[5] Id.

Dr. Gans also disagreed with Dr. Durvasula's characterization of R.F.'s episodes as "sepsis-like" or as an episode of systemic inflammatory response syndrome ("SIRS"). She noted that neither sepsis nor SIRS self-resolve in a few hours, as routinely occurred in R.F.'s case. Resp't's Ex. A, at 5. And SIRS, she said, is not a recurrent condition. Id. Dr. Gans also emphasized that "the onset of a chronic illness, even forms of immunodeficiency, are insidious and develop over time with inciting events before their onset and a different reaction once the condition manifests." Id. As such, Dr. Gans emphasized that the immunologists who saw R.F. in

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[4] Dr. Gans received a bachelor's degree in biochemistry from Connecticut College and her medical degree from SUNY Health Science Center at Syracuse. Resp't's Ex. B, at 1, ECF No. 46-8. She completed an internship and residency program in the Department of Pediatrics and a fellowship in the Division of Pediatric Infectious Diseases at Stanford University School of Medicine. Id. Dr. Gans currently works as a clinical professor and Director of Fellowship Education in the Department of Pediatrics, and the Fellowship Associate Program Director of Pediatrics Infectious Diseases at Stanford University Medical Center. Id. Dr. Gans has published 30 peer-reviewed articles, nine book chapters, and 34 abstracts. Id. at 5–10.

[5] The "allergy/immunology physician" to whom Dr. Gans referred appears to be Dr. Tongchinsub. See Resp't's Ex. C, at 1 (citing Pet'rs' Ex. 21, at 1–3). As described above, she opined that it was "unlikely" that R.F.'s constellation of symptoms was caused by a vaccine, because his subsequent episodes recurred without the incitement of a vaccine. Pet'rs' Ex. 21, at 3.

2017 and 2018 were better able to understand R.F.'s chronic condition than Dr. Oppenheimer, who saw R.F. in 2014. Id.

Dr. Gans further asserted that Dr. Durvasula's report was flawed in that it provided "no biologic plausible explanation" to explain "how a hyper immune response to [a] Hepatitis B vaccine would cause a hyperimmune response to subsequent unrelated infectious exposures." Id. In addition, she criticized Dr. Durvasula's reliance on publications that were inapposite because they involved different conditions, and the reactions described in the literature did not fit R.F.'s history. See id. at 5–6.

Dr. Gans concluded that "[R.F.'s] episodes are a result of a predisposing condition and are not dependent on any specific inciting event, as is the rule with chronic conditions." Id. at 6. Further, she said, "[t]here is no biologic plausibility to one specific insult causing a condition that recurs upon exposure to unrelated insults, and no data to support the receipt of a vaccine with a chronic recurring condition." Id. at 6.

Dr. Gans also questioned whether R.F.'s episodes were actually associated with his viral illnesses. See Resp't's Ex. C, at 2. She opined that "RF has an underlying condition, the cause of which is likely genetic, with manifestations after variable triggers." Id. at 3. She stated further that "[t]hese triggers do cause the clinical signs and symptoms but do not cause the underlying condition." Id. In short, she explained, while the vaccine "was only temporally associated with one of many events," "the cause of RF's recurring episodes can be explained entirely by an underlying condition which is entirely independent of the vaccine." Id. at 3–4.

C. The Special Master's Opinion

The special master conducted a detailed review of R.F.'s medical records and a comprehensive analysis of the expert reports and the medical literature, which he discussed at length in his opinion. See Dec. at 17–21. He concluded, in agreement with Dr. Gans, that Petitioners failed to present sufficient evidence in support of their theory that the hepatitis B vaccine "can cause a hypersensitivity reaction that would in turn cause chronic immune dysregulation resulting in episodic presentations of hypothermia, unresponsiveness, and hypotonia, coupled with diffuse osteopenia." Id. at 21. He therefore found that Petitioners had failed to meet their burden of supplying a medical theory of causation that is "supported by sound and reliable medical or scientific explanation." See Knudsen ex rel. Knudsen, 35 F.3d at 548.

As the special master observed, Dr. Durvasula characterized R.F.'s initial reaction to the hepatitis B vaccine as a hypersensitivity response. Dec. at 17–18. He noted that Dr. Durvasula had opined that the response caused R.F. to suffer similar subsequent episodes that, unlike his initial reaction, were triggered by viral illnesses. Id. (citing Pet'rs' Ex. 22, at 4). The special master found this theory was not supported by a sound and reliable scientific explanation. He noted Dr. Gans's observations that "hypersensitivity reactions and SIRS are acute responses that do not present chronically and/or episodically" and that "hypersensitivity responses are antigen-specific." Dec. at 18 (citing Resp't's Ex. C, at 2–3). "[H]ypersensitivity alone [did] not explain R.F.'s episodic presentation," the special master reasoned, "given that the later episodes were triggered by other unspecified viral illnesses." Id. Quoting Dr. Gans, the special master observed

that "there is no biologic condition where one trigger, e.g. a vaccine, causes a 'normal' response to suddenly chronically dysregulate so that all subsequent unrelated exposures cause the same dysregulation." Id. (quoting Resp't's Ex. C, at 2). In the special master's view, Dr. Durvasula "glosse[d] over the details of the proposed relationship between hypersensitivity and autoimmunity" and did not fully "articulate[] how R.F.'s alleged post-vaccination hypersensitivity reaction could have led to the chronic state of immune dysregulation he posits." Id.

Further, Dr. Durvasula had relied on the Agmon-Levin article for the proposition that "autoimmunity can arise in susceptible individuals as a result of environmental triggers, including from vaccine antigens." Id. (referring to Pet'rs' Ex. 26). But the article did not specifically discuss the hepatitis B vaccine nor any condition that matched R.F.'s symptoms. See Pet'rs' Ex. 26. Moreover, the Special Master observed, even accepting Dr. Durvasula's theory that a vaccine could result in hypersensitivity leading to autoimmunity, Dr. Durvasula's ultimate reliance on autoimmunity in this case "would still be unsupported ipse dixit that cannot be credited." Dec. at 19. The special master acknowledged that "[t]here is no question that autoimmunity is an established category of disease that can, in at least some instances, be linked to vaccination." Id. (citing 42 C.F.R. § 100.3(b)(15)). "However," the special master noted, "there are various pathways to autoimmunity and many autoimmune conditions have little to no suspicion of vaccine causation." Id. "Despite invoking the concept as the sole explanation for the chronic immune dysregulation he posits," the special master found, "Dr. Durvasula has not substantiated that autoimmunity is relevant to this case and has not sufficiently articulated a theory based in autoimmunity." Id.

The special master also found Dr. Durvasula's theory unsupported because he did not identify which type of hypersensitivity R.F. experienced, id. at 18 (citing Pet'rs' Ex. 30, at 4), nor which autoimmune disorder R.F. suffers from or even might suffer from, id. at 19 ("[M]edical recognition of the injury claimed is critical and by definition a 'vaccine-related injury,' . . . has to be more than just a symptom or manifestation of an unknown injury." (quoting Broekelschen, 618 F.3d at 1349)).

The special master acknowledged that Dr. Durvasula had referenced the possibility that "hypersensitivity can result in cross reaction and molecular mimicry, which is a known mechanism of autoimmunity." Dec. at 20. He also acknowledged that "[m]olecular mimicry 'is a generally accepted scientific principle,'" but noted that its "mere invocation" was not sufficient to carry Petitioners' burden to show causation. Id. (quoting Deshler v. Sec'y of Health & Hum. Servs., 2020 WL 4593162, 2020 U.S. Claims LEXIS 1418 (Fed. Cl. July 1, 2020)). Further, the special master observed that Dr. Durvasula "[did] not identify any proposed homology, any relevant autoantibody, or even explain what specific autoimmune target within the body would be responsible for [R.F.'s symptoms]." Id. In short, the Special Master found Dr. Durvasula's analysis was "too vague to preponderantly support a theory of causation." Id.

D. Petitioners' Prong One Arguments

As the foregoing shows, the special master discussed the evidence at length, explaining why he gave greater weight to the opinions of the government's expert, Dr. Gans, than to those of Petitioners' expert, Dr. Durvasula. See Dec. at 17–21. He concluded that there was a "dearth"

of evidence or explanation supporting Dr. Durvasula's opinion that hepatitis B vaccine could cause a hypersensitivity reaction that would result in chronic immune system dysregulation leading to episodes of hypothermia, unresponsiveness, and hypotonia. Id. at 21. And for that reason, he found that Petitioners had not met their burden as to general causation under Althen prong 1.

In their motion for review, Petitioners cast these determinations as legally erroneous. However, Petitioners' objections are not grounded in the law; they are grounded in a disagreement about the weight the special master assigned to the evidence upon which the parties relied. See Pet'rs' Mem. at 34–39. Their objections are therefore subject to the "uniquely deferential" standard of review applicable to a special masters' findings of fact.

Petitioners have not shown that the special master's determination that they failed to satisfy prong one was arbitrary and capricious or an abuse of discretion. In fact, the section of their brief that addresses prong one consists largely of lengthy block quotes from Dr. Durvasula's expert reports. Id. at 37–38. Petitioners also reference and quote at length a passage from the court's decision in Caves v. Sec'y of Health & Hum. Servs., which held that petitioners must supply something more than a "plausible" theory to meet their burden of proof under Althen prong one. Id. at 35–36 (quoting 100 Fed. Cl. 119, 143 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012)).

As best the Court can follow their argument, it appears that Petitioners' main critique of the special master's ruling on prong one concerns the impact that the absence of a definitive diagnosis had on his reasoning. Petitioners imply that, in finding that they lacked a reliable theory of causation, the special master improperly depended upon the fact that R.F. was diagnosed with an "unspecified" disorder of the immune system. See id. at 39.

As Petitioners note, the special master commented that because a specific autoimmune disorder had not been identified it would be "speculative" to determine that the cause of the disorder was R.F.'s reaction to the vaccine, as opposed to a condition that pre-existed his receipt of the vaccine. Dec. at 26. But this was by no means the sole or even principal reason the special master found that Petitioners failed to satisfy prong 1.

To the contrary, as described above, the special master found Dr. Durvasula's theory unsupported because he had "glosse[d] over the details of the proposed relationship between hypersensitivity and autoimmunity." Id. at 18. In addition, Dr. Durvasula did not "clarify what type of hypersensitivity he [invoked]." Id. (citing Pet'rs' Ex. 30). Further, Dr. Durvasula relied on medical literature to support his claim that hypersensitivity can lead to autoimmunity, but that literature did not discuss the hepatitis B vaccine nor any autoimmune condition similar to R.F.'s. Id.; see also Pet'rs' Ex. 30 (quoting Pet'rs' Ex. 26). And Dr. Durvasula did not "identif[y] any autoimmune pathway [that] could theoretically result in [R.F.'s symptoms]." Dec. at 19.

In addition, the special master based his determination on Dr. Gans's observations that hypersensitivity responses are antigen-specific, that "there is no biologic condition where one trigger, e.g. a vaccine, causes a 'normal' response to suddenly chronically dysregulate so that all subsequent unrelated exposures cause the same dysregulation," and that "hypersensitivity

reactions and SIRS are acute responses that do not present chronically and/or episodically." Dec. at 18 (quoting Resp't's Ex. C, at 2–3). The special master found that all of these observations undermined Petitioners' arguments.

As the court of appeals has observed, in vaccine cases "[t]he special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories." Broekelschen, 618 F.3d at 1347 (citing Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357, 1362 (Fed. Cir. 2000)). In such cases, "[t]he statute makes clear that, on review, the Court of Federal Claims is not to second guess the Special Masters fact-intensive conclusions." Milik, 822 F.3d at 1376 (quoting Hodges, 9 F.3d at 961). Petitioners have not persuaded the Court that the special master abused his discretion in crediting the opinions of the government's expert over those of their own. And because they have failed to satisfy Althen prong one, their motion for review must be denied.

CONCLUSION

For the foregoing reasons, the special master's determination that Petitioners failed to satisfy Althen prong one was neither arbitrary and capricious, nor contrary to law. Petitioners' motion for review is therefore **DENIED** and the decision of the special master is **SUSTAINED**. The Clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/ Elaine D. Kaplan
ELAINE D. KAPLAN
Chief Judge